FEZ1 is an intrinsically unfolded protein, acts in concert with NEK1 and CLASP2 at centrossomes and provokes the “flower like” phenotype in human cells

Lanza, D.C.F.[1,2], Silva,J.C. [1,3], Meirelles,G. A. [1,2], Alborghetti,M. R. [1,2], Assmann,E. M.[1], Trindade,D.M. [1,2],Quaresma,A.J.C. [1,2], Bressan,G.C. [1,2], Torriani,I.L. [1,3], Lenz,G. [4], Kobarg,J. [1,2].

[1]LNLS, Campinas, SP, Brazil, [2]Instituto de Biologia, UNICAMP, SP, Brazil, [3]Instituto de Física, UNICAMP, SP, Brazil, [4]Instituto de Biologia, UFRGS, Brazil.

The Fasciculation and Elongation protein Zeta1 (FEZ1) is the mammalian orthologue of the *C. elegans* protein UNC-76, necessary for axon growth. Our experiments of circular dichroism, fluorescence spectroscopy and limited proteolysis suggest that FEZ1 contains disordered regions. Pull down and SAXS experiments confirmed that FEZ1 dimerizes in N-terminus. Shape analysis using SAXS data proved that FEZ1 is a dimer of elongated shape. We further performed *in vitro* phosphorylation assays of FEZ1 and found that phosphorylation occurred mainly in its C-terminal region and inhibited FEZ1 interaction with CLASP2 *in vitro*. Furthermore, we over-expressed GFP-FEZ1 in human cells and observed that 40% of transfected cells develop “flower-like” nuclei. We further demonstrated that GFP-FEZ1 localizes to both the cytoplasm and the nucleus, and that the appearance of the nuclei depends on intact microtubules. In the center of the “flower nuclei” FEZ1 co-localizes with alpha and gamma tubulin. Finally, we observed that FEZ1 interacts and co-localizes with NEK1 and CLASP2 to the centrossome in a phosphorylation dependent way. Its interactions occur by coiled coil specific contacts. Concluding, our data suggest that FEZ1 is a natively unfolded protein and that it´s interaction and transport functions may be subject to regulation by phosphorylation. FEZ1, NEK1 and CLASP2 together, seems to have an important centrosomal functions and the study of their interplay may supply new mechanistic insights to the formation of "flower-like"nuclei, witch are a phenotypical hallmark of human leukemia cells.

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